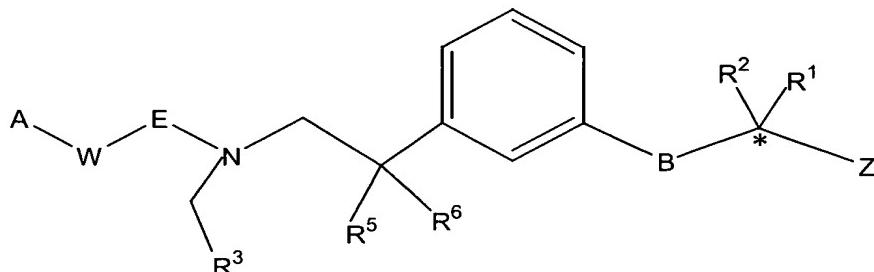


CLAIMS

1. A compound of the Formula I

5



Formula I

a prodrug therof, or a pharmaceutically acceptable salt of said compound or of said prodrug;

10 wherein

E is carbonyl or sulfonyl;

B is oxy, thio, sulfinyl, sulfonyl, methylene, or -N(H)-;

Z is carboxyl, carboxaldehyde, hydroxymethyl, (C₁-C₄)alkoxycarbonyl, cyano, hydroxyaminocarbonyl, tetrazolyl, tetrazolylaminocarbonyl, 4,5-dihydro-5-oxo-1,2,4-

15 oxadiazol-3-yl, 3-oxoisoxazolidin-4-yl-aminocarbonyl, or -C(O)N(H)SO₂R⁴,

where R⁴ is (C₁-C₆)alkyl, amino or mono-N- or di-N,N-(C₁-C₆)alkylamino said (C₁-C₆)alkyl substituents are optionally substituted independently with from one to nine fluorines;

W is a bond, -N(H)-, (C₁-C₄)alkylamino, -N((C₁-C₄)alkyl)- or (C₁-C₈)alkylene;

20 wherein said (C₁-C₈)alkylene may optionally be mono- or di-substituted

independently with oxo, halo, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₃-C₇)cycloalkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, cyano, nitro, or mono-N- or di-N,N-(C₁-C₆)alkylamino or

25 wherein W is CR⁷R⁸ wherein R⁷ and R⁸ are linked together to form a three to six membered fully saturated carbocyclic ring;

R¹ is H, (C₁-C₄)alkyl or (C₃-C₆)cycloalkyl;

R² is H, a (C₃-C₆)cycloalkyl or a fully saturated, partially unsaturated or fully unsaturated one to four membered straight or branched carbon chain wherein the carbon(s) may optionally be replaced with one or two heteroatoms selected independently from oxygen and sulfur and wherein said carbon(s) is optionally mono-, di- or tri-substituted independently with halo, said carbon(s) is optionally mono-substituted with hydroxy, said carbon(s) is optionally mono-substituted with oxo, said sulfur is optionally mono- or di-substituted with oxo, and said chain is optionally mono-substituted with Y;

- wherein Y is a partially saturated, fully saturated or fully unsaturated three to eight membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, said bicyclic ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen;
- wherein said Y ring is optionally mono-, di- or tri-substituted independently with halo, (C₂-C₆)alkenyl, (C₁-C₆) alkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, cyano, oxo, carboxy, (C₁-C₆)alkyloxycarbonyl, mono-N- or di-N,N-(C₁-C₆)alkylamino wherein said (C₁-C₆)alkyl substituent is optionally mono-, di- or tri-substituted independently with halo, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, cyano, oxo, carboxy, (C₁-C₆)alkyloxycarbonyl, mono-N- or di-N,N-(C₁-C₆)alkylamino, said (C₁-C₆)alkyl substituent is also optionally substituted with from one to nine fluorines; or
- R¹ and R² are linked together to form a three to six membered fully saturated carbocyclic ring optionally having one heteroatom selected from oxygen, sulfur and nitrogen;
- R³ is (C₁-C₁₀)alkyl, (C₂-C₁₀)alkenyl or (C₂-C₁₀)alkynyl, said (C₁-C₁₀)alkyl, (C₂-C₁₀)alkenyl or (C₂-C₁₀)alkynyl substituents are optionally mono-, di- or tri-substituted independently with halo, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, cyano, oxo, carboxy, (C₁-C₆)alkyloxycarbonyl, or mono-N- or di-N,N-(C₁-C₆)alkylamino or optionally
- said (C₁-C₁₀)alkyl, (C₂-C₁₀)alkenyl or (C₂-C₁₀)alkynyl substituents are mono-substituted with a partially saturated, fully saturated or fully unsaturated five to six membered ring optionally having one to two heteroatoms selected from nitrogen, oxygen and sulfur, or a bicyclic ring consisting of two fused partially saturated, fully

saturated or fully unsaturated three to six membered rings, taken independently, said bicyclic ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen

- said ring optionally mono-, di- or tri-substituted independently with halo, (C₂-C₆)alkenyl, (C₁-C₆) alkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, cyano, oxo, carboxy, (C₁-C₆)alkyloxycarbonyl, mono-N- or di-N,N-(C₁-C₆)alkylamino wherein said (C₁-C₆)alkyl substituent is optionally mono-, di- or tri-substituted independently with halo, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, cyano, oxo, carboxy, (C₁-C₆)alkyloxycarbonyl, mono-N- or di-N,N-(C₁-C₆)alkylamino, said (C₁-C₆)alkyl substituent is also optionally substituted with from one to nine fluorines;
- R⁵ and R⁶ are linked together to form a three to six membered fully saturated carbocyclic ring or are each independently H, (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl or (C₃-C₇)cycloalkyl(C₁-C₆)alkyl; and
- A is H, mono-N- or di-N,N-(C₁-C₆)alkylamino, (C₂-C₆)alkanoylamino, (C₁-C₆)alkoxy, or a partially saturated, fully saturated or fully unsaturated three to eight membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, said bicyclic ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen; and
- wherein said A ring is optionally mono-, di- or tri-substituted independently with oxo, carboxy, halo, (C₁-C₆)alkyloxycarbonyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₃-C₇)cycloalkyl, (C₃-C₇)cycloalkyl(C₁-C₆)alkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, cyano, nitro, or mono-N- or di-N,N-(C₁-C₆)alkylamino wherein said (C₁-C₆)alkyl and (C₁-C₆)alkoxy substituents are also optionally mono-, di- or tri-substituted independently with halo, hydroxy, (C₁-C₆)alkoxy, amino, mono-N- or di-N,N-(C₁-C₆)alkylamino or from one to nine fluorines or
- wherein said A ring is optionally mono-substituted with a partially saturated, fully saturated or fully unsaturated three to eight membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen.

2. A compound as recited in claim 1 wherein

E is C(O);

B is oxy;

Z is carboxy;

W is a bond, (C_1 - C_4)alkylene, or -N(H)- wherein said (C_1 - C_4)alkylene may optionally be mono- or di-substituted independently with (C_1 - C_4)alkyl, (C_1 - C_4)alkoxy or (C_3 - C_7)cycloalkyl;

R¹ is H, (C_1 - C_4)alkyl or (C_3 - C_6)cycloalkyl;

5 R² is H, (C_1 - C_4)alkyl, or (C_3 - C_6)cycloalkyl;

R³ is (C_4 - C_8)alkyl;

R⁵ and R⁶ are each H;

A is a five to six membered partially saturated, fully saturated or fully unsaturated ring optionally having one heteroatom selected from oxygen, sulfur and nitrogen, or a

10 bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated five to six membered ring, taken independently, optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said A substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy, (C_1 - C_4)alkylthio, amino,

15 nitro, cyano or mono-N- or di-N,N-(C_1 - C_6)alkylamino said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy substituents are also optionally substituted independently with from one to nine fluorines or a pharmaceutically acceptable salt thereof.

3. A compound as recited in claim 2 wherein

W is a bond, (C_1 - C_4)alkylene, or -N(H)-;

20 R¹ and R² are each independently H, or (C_1 - C_4)alkyl;

A is phenyl, wherein said phenyl substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy, (C_1 - C_4)alkylthio, amino, nitro, cyano or mono-N- or di-N,N-(C_1 - C_6)alkylamino said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy substituents are also optionally substituted independently with from one to nine

25 fluorines or a pharmaceutically acceptable salt thereof.

4. A compound as recited in claim 3 wherein

W is methylene;

R¹ and R² are each independently H or (C_1 - C_2)alkyl;

said A phenyl substituent is optionally mono- or di-substituted independently with

30 fluoro, trifluoromethyl, trifluoromethoxy, chloro, (C_1 - C_3)alkyl, hydroxy, (C_1 - C_2)alkoxy, amino or mono-N- or di-N,N-(C_1 - C_2)alkylamino; and

R³ is (C_6 - C_8)alkyl or the pharmaceutically acceptable salts thereof.

5. A compound as recited in claim 1 wherein said compound is

(R)-2-[3-(2-[(2,5-dimethoxy-phenyl)-acetyl]-heptyl-amino}-ethyl]-phenoxy]-2-methylbutyric acid;

(S)-2-[3-(2-[(2,5-dimethoxy-phenyl)-acetyl]-heptyl-amino}-ethyl]-phenoxy]-2-methylbutyric acid;

5 (R)-2-[3-(2-{heptyl-[(4-hydroxy-phenyl)-acetyl]-amino}-ethyl)-phenoxy]-2-methylbutyric acid;

(S)-2-[3-(2-{heptyl-[(4-hydroxy-phenyl)-acetyl]-amino}-ethyl)-phenoxy]-2-methylbutyric acid;

or the pharmaceutically acceptable salts of said compounds.

10 6. A compound as recited in claim 4 wherein said compound is

a. R¹ is methyl;

R² is ethyl;

R³ is heptyl; and

A is 2,5-dimethoxyphenyl; or

15 b. R¹ is methyl;

R² is ethyl;

R³ is heptyl; and

A is 4-hydroxyphenyl or the pharmaceutically acceptable salts of said compounds.

7. A compound as recited in claim 3 wherein

20 W is -N(H)-;

R¹ and R² are each independently H or (C₁-C₂)alkyl;

said A phenyl substituent is optionally mono- or di-substituted independently with fluoro, trifluoromethyl, trifluoromethoxy chloro, (C₁-C₃)alkyl, hydroxy, (C₁-C₂)alkoxy, amino or mono-N- or di-N,N-(C₁-C₂)alkylamino; and

25 R³ is (C₄-C₈)alkyl or a pharmaceutically acceptable salt thereof.

8. A compound as recited in claim 1 wherein said compound is

(R)-2-(3-{2-[3-(4-ethyl-phenyl)-1-heptyl-ureido]-ethyl}-phenoxy)-2-methylbutyric acid;

(S)-2-(3-{2-[3-(4-ethyl-phenyl)-1-heptyl-ureido]-ethyl}-phenoxy)-2-methylbutyric acid;

(R)-2-(3-{2-[1-heptyl-3-(4-trifluoromethoxy-phenyl)-ureido]-ethyl}-phenoxy)-2-methyl-

30 butyric acid;

(S)-2-(3-{2-[1-heptyl-3-(4-trifluoromethoxy-phenyl)-ureido]-ethyl}-phenoxy)-2-methylbutyric acid;

2-(3-{2-[3-(2,4-difluoro-phenyl)-1-heptyl-ureido]-ethyl}-phenoxy)-2-ethylbutyric acid;

- 2-(3-{2-[3-(2,4-dimethoxy-phenyl)-1-heptyl-ureido]-ethyl}-phenoxy)-2-ethyl-butyric acid;
- 2-(3-{2-[1-heptyl-3-(4-isopropyl-phenyl)-ureido]-ethyl}-phenoxy)-2-methyl-propionic acid;
- 5 (R)-2-(3-(2-[1-heptyl-3-(4-isopropyl-phenyl)ureido]-ethyl)-phenoxy)-2-methyl-butyric acid;
- (S)-2-(3-(2-[1-heptyl-3-(4-isopropyl-phenyl)ureido]-ethyl)-phenoxy)-2-methyl-butyric acid;
- or the pharmaceutically acceptable salts of said compounds.
- 10 9. A compound as recited in claim 7 wherein
- a. R¹ is methyl;
 - R² is ethyl;
 - R³ is heptyl; and
 - A is 4-ethylphenyl;
- 15 b. R¹ is methyl;
- R² is ethyl;
 - R³ is heptyl; and
 - A is 4-trifluoromethoxyphenyl;
- c. R¹ is ethyl;
- 20 R² is ethyl;
- R³ is heptyl; and
 - A is 2,4-difluorophenyl;
- d. R¹ is ethyl;
- R² is ethyl;
- 25 R³ is heptyl; and
- A is 2,4-dimethoxyphenyl;
- e. R¹ is methyl;
- R² is methyl;
 - R³ is heptyl; and
- 30 A is 4-isopropylphenyl;
- f. the stereochemistry of C⁷ is R;
- R¹ is methyl;
 - R² is ethyl;
 - R³ is heptyl; and

A is 4-isopropylphenyl; or

g. the stereochemistry of C is S;

R¹ is methyl;

R² is ethyl;

5 R³ is heptyl; and

A is 4-isopropylphenyl

or the pharmaceutically acceptable salts of said compounds.

10. A compound as recited in claim 1 wherein

E is C(O);

10 B is C(H)₂;

Z is carboxy;

W is a bond or -N(H)-;

R¹ is H, (C₁-C₄)alkyl or (C₃-C₆)cycloalkyl;

R² is H, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)alkylthio, phenoxy, phenylmethoxy,

15 phenylthio, phenylmethylthio, or (C₃-C₆)cycloalkyl, said phenyl moieties optionally mono-or di-substituted independently with cyano, fluoro, trifluoromethyl, trifluoromethoxy, chloro, (C₁-C₃)alkyl, hydroxy, (C₁-C₂)alkoxy, amino or mono-N- or di-N,N-((C₁-C₂)alkylamino;

R³ is (C₄-C₈)alkyl;

20 R⁵ and R⁶ are each H;

A is a five to six membered partially saturated, fully saturated or fully unsaturated ring optionally having one heteroatom selected from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated five to six membered rings, taken independently, optionally having one to 25 four heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said A substituent is optionally mono-, di- or tri-substituted independently with halo, (C₁-C₆) alkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, cyano, or mono-N- or di-N,N-(C₁-C₆)alkylamino, said (C₁-C₆)alkyl or (C₁-C₆)alkoxy substituents are optionally substituted independently with from one to nine fluorines or a pharmaceutically acceptable salt thereof.

30 11. A compound as recited in claim 1 wherein

E is S(O)₂;

B is oxy;

Z is carboxy;

W is a bond, (C_1 - C_4)alkylene, (C_1 - C_4)alkylamino or -N(H)- wherein said (C_1 - C_4)alkylene may optionally be mono- or di-substituted independently with (C_1 - C_4)alkyl, (C_1 - C_4)alkoxy or (C_3 - C_6)cycloalkyl;

R¹ is H, (C_1 - C_4)alkyl or (C_3 - C_6)cycloalkyl;

5 R² is H, (C_1 - C_4)alkyl, (C_1 - C_4)alkoxy or (C_3 - C_6)cycloalkyl;

R³ is (C_4 - C_8)alkyl;

R⁵ and R⁶ are each H;

A is a five to six membered partially saturated, fully saturated or fully unsaturated ring optionally having one heteroatom selected from oxygen, sulfur and nitrogen, or a

10 bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated five to six membered ring, taken independently, optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said A substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy, (C_1 - C_4)alkylthio, amino,

15 nitro, or mono-N- or di-N,N-(C_1 - C_6)alkylamino, said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy substituents are optionally substituted independently with from one to nine fluorines or a pharmaceutically acceptable salt thereof.

12. A compound as recited in claim 11 wherein

W is a bond, (C_1 - C_4)alkylene, or -N(H)-;

20 R¹ and R² are each independently H or (C_1 - C_4)alkyl;

A is phenyl, wherein said phenyl substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy, (C_1 - C_4)alkylthio, amino, nitro, cyano, or mono-N- or di-N,N-(C_1 - C_6)alkylamino said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy substituents are optionally substituted independently with from one to nine

25 fluorines or a pharmaceutically acceptable salt thereof.

13. A compound as recited in claim 12 wherein

W is methylene or -N(H)-;

R¹ and R² are each independently H or (C_1 - C_2)alkyl;

A is phenyl; wherein

30 said phenyl is optionally mono- or di-substituted independently with fluoro,

trifluoromethyl, chloro, cyano, (C_1 - C_3)alkyl, hydroxy, (C_1 - C_2)alkoxy, amino or mono-N- or di-N,N-(C_1 - C_2)alkylamino;

R³ is (C_6 - C_8)alkyl or a pharmaceutically acceptable salt thereof.

14. A compound as recited in claim 1 wherein

E is C(O);

B is thio;

Z is carboxy;

W is a bond, (C₁-C₄)alkylene, (C₁-C₄)alkylamino or -N(H)- wherein said (C₁-

5 C₄)alkylene may optionally be mono- or di-substituted independently with (C₁-C₄)alkyl, (C₁-C₄)alkoxy or (C₃-C₇)cycloalkyl;

R¹ is H, (C₁-C₄)alkyl or (C₃-C₆)cycloalkyl;

R² is H, (C₁-C₄)alkyl or (C₃-C₆)cycloalkyl;

R³ is (C₄-C₈)alkyl;

10 R⁵ and R⁶ are each H;

A is a five to six membered partially saturated, fully saturated or fully unsaturated ring optionally having one heteroatom selected from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated five to six membered rings, taken independently, optionally having one to

15 four heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said A substituent is optionally mono-, di- or tri-substituted independently with halo, (C₁-C₆) alkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, or mono-N- or di-N,N-(C₁-C₆)alkylamino said (C₁-C₆)alkyl or (C₁-C₆)alkoxy substituents are optionally substituted independently with from one

20 to nine fluorines or a pharmaceutically acceptable salt thereof.

15. A compound as recited in claim 14 wherein

A is phenyl, wherein said phenyl substituent is optionally mono-, di- or tri-substituted independently with halo, cyano, (C₁-C₆) alkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, or mono-N- or di-N,N-(C₁-C₆)alkylamino said (C₁-C₆)alkyl or (C₁-

25 C₆)alkoxy substituents are optionally substituted independently with from one to nine fluorines or a pharmaceutically acceptable salt thereof.

16. A compound as recited in claim 15 wherein

W is methylene or N(H);

R¹ and R² are each independently H or (C₁-C₂)alkyl;

30 A is phenyl; wherein

said phenyl is optionally mono- or di-substituted independently with fluoro, trifluoromethyl, chloro, (C₁-C₃)alkyl, hydroxy, (C₁-C₂)alkoxy, amino or mono-N- or di-N,N-(C₁-C₂)alkylamino; and

R³ is (C₆-C₈)alkyl or a pharmaceutically acceptable salt thereof.

17. A compound as recited in claim 1 wherein said compound is
2-(3-{2-[3-(4-isopropyl-phenyl)-1-heptyl-ureido]-ethyl}-phenylsulfanyl)-2-methyl-
propionic acid;
2-(3-{2-[3-(2,4-difluoro-phenyl)-1-heptyl-ureido]-ethyl}-phenylsulfanyl)-2-methyl-
5 propionic acid;
2-(3-{2-[3-(2,4-dimethoxy-phenyl)-1-heptyl-ureido]-ethyl}-phenylsulfanyl)-2-methyl-
propionic acid;
or the pharmaceutically acceptable salts of said compounds.

18. A compound as recited in claim 16 wherein

- 10 a. W is N(H);
 R^1 is methyl;
 R^2 is methyl;
 R^3 is heptyl; and
A is 2,4-difluorophenyl;
- 15 b. W is N(H);
 R^1 is methyl;
 R^2 is methyl;
 R^3 is heptyl; and
A is 2,4-dimethoxyphenyl

20 or the pharmaceutically acceptable salts of said compounds.

19. A compound as recited in claim 1 wherein

E is C(O) or S(O)₂;

B is oxy or thio;

Z is carboxy;

25 W is (C₁-C₈)alkylene;

R^1 and R^2 are each independently H, (C₁-C₄)alkyl or (C₃-C₆)cycloalkyl;

R^3 is a five to six membered partially saturated, fully saturated or fully unsaturated ring optionally having one or two heteroatoms selected from nitrogen, oxygen and sulfur, said ring optionally linked via (C₁-C₈)alkylene and said ring optionally mono-, di- or tri-substituted independently with halo, (C₁-C₆) alkyl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₄)alkylthio, amino, nitro, or mono-N- or di-N,N-(C₁-C₆)alkylamino said (C₁-C₆)alkyl or (C₁-C₆)alkoxy substituents are optionally substituted independently with from one to nine fluorines;

R^5 and R^6 are each H;

- A is a five to six membered partially saturated, fully saturated or fully unsaturated ring optionally having one heteroatom selected from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated five to six membered rings, taken independently, optionally having one to
- 5 four heteroatoms selected independently from oxygen, sulfur and nitrogen;
- wherein said A substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy, (C_1 - C_4)alkylthio, amino, nitro, cyano, or mono-N- or di-N,N-(C_1 - C_6)alkylamino, said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy substituents are optionally substituted independently with from one to nine
- 10 fluorines or a pharmaceutically acceptable salt thereof.
20. A compound as recited in claim 19 wherein
- R^3 is phenyl(C_1 - C_4)alkyl, said phenyl optionally mono-, di- or tri-substituted independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy, (C_1 - C_4)alkylthio, amino, nitro, or mono-N- or di-N,N-(C_1 - C_6)alkylamino, said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy
- 15 substituents are also optionally substituted independently with from one to nine fluorines or a pharmaceutically salt thereof.
21. A compound as recited in claim 19 wherein
- E is $C(O)$; and
- B is oxy or a pharmaceutically acceptable salt thereof.
- 20 22. A compound as recited in claim 19 wherein
- E is $S(O)_2$; and
- B is oxy or a pharmaceutically acceptable salt thereof.
23. A compound as recited in claim 1 wherein
- A is phenyl, wherein said phenyl substituent is optionally mono-, di- or tri-substituted
- 25 independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy, (C_1 - C_4)alkylthio, amino, nitro, cyano, or mono-N- or di-N,N-(C_1 - C_6)alkylamino, said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy substituents are optionally substituted independently with from one to nine fluorines or a pharmaceutically acceptable salt thereof.
24. A compound as recited in claim 1 wherein
- 30 E is $C(O)$ or $S(O)_2$;
- B is oxy or thio;
- Z is carboxy;
- W is $N(H)$, (C_1 - C_8)alkylamino or (C_1 - C_8) alkylene;
- R^1 and R^2 are each independently H, (C_1 - C_4)alkyl or (C_3 - C_6)cycloalkyl;

R^3 is a five to six membered partially saturated, fully saturated or fully unsaturated ring optionally having one or two heteroatoms selected from nitrogen, oxygen and sulfur, said ring optionally linked via (C_1 - C_8)alkylene and said ring optionally mono-, di- or tri-substituted independently with halo, (C_1 - C_6) alkyl, hydroxy, (C_1 - C_6)alkoxy,

- 5 (C_1 - C_4)alkylthio, amino, nitro, or mono-N- or di-N,N-(C_1 - C_6)alkylamino said (C_1 - C_6)alkyl or (C_1 - C_6)alkoxy substituents are optionally substituted independently with from one to nine fluorines;

R^5 and R^6 are each H; and

A is H or a pharmaceutically acceptable salt thereof.

- 10 25. A compound as recited in claim 24 wherein

E is C(O); and

B is oxy or a pharmaceutically acceptable salt thereof.

26. A compound as recited in claim 1 wherein said compound is:

(R)-2-[3-(2-{1-[2-(2,4-difluoro-phenyl)-ethyl]-3-pentyl-ureido}-ethyl)-phenoxy]-2-

- 15 methyl-butyric acid;

(S)-2-[3-(2-{1-[2-(2,4-difluoro-phenyl)-ethyl]-3-pentyl-ureido}-ethyl)-phenoxy]-2-methyl-butyric acid;

(R)-2-[3-(2-{1-[2-(2,4-difluoro-phenyl)-ethyl]-3-hexyl-ureido}-ethyl)-phenoxy]-2-methyl-butyric acid; or

- 20 (S)-2-[3-(2-{1-[2-(2,4-difluoro-phenyl)-ethyl]-3-hexyl-ureido}-ethyl)-phenoxy]-2-methyl-butyric acid;

or a pharmaceutically acceptable salt of said compounds.

27. A compound as recited in claim 25 wherein

a. W is hexylamino;

- 25 R^1 is methyl;

R^2 is ethyl;

R^3 is 2,4-difluorobenzyl;

b. W is pentylamino;

R^1 is methyl;

- 30 R^2 is ethyl;

R^3 is 2,4-difluorobenzyl;

or the pharmaceutically salts of said compounds.

28. A method for treating obesity, overweight condition, hypertriglyceridemia, hyperlipidemia, hypoalphalipoproteinemia, Syndrome X, diabetes mellitus (Type I

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- and/or Type II), hyperinsulinemia, impaired glucose tolerance, insulin resistance, diabetic complications, atherosclerosis, hypertension, coronary heart disease, hypercholesterolemia, inflammation, thrombosis or congestive heart failure in a mammal by administering to a mammal in need of such treatment a therapeutically effective amount of a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug.
- 5 29. A method as recited in claim 28 wherein atherosclerosis is treated.
30. A method as recited in claim 28 wherein peripheral vascular disease is treated.
31. A method as recited in claim 28 wherein dyslipidemia is treated.
- 10 32. A method as recited in claim 28 wherein diabetes is treated.
33. A method as recited in claim 28 wherein hypoalphalipoproteinemia is treated.
34. A method as recited in claim 28 wherein hypercholesterolemia is treated.
35. A method as recited in claim 28 wherein hypertriglyceridemia is treated.
36. A method as recited in claim 28 wherein obesity is treated.
- 15 37. A pharmaceutical composition which comprises a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug and a pharmaceutically acceptable carrier, vehicle or diluent.
38. A pharmaceutical composition for the treatment of atherosclerosis in a mammal which comprises an atherosclerosis treating amount of a compound of claim 1, a
- 20 prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug and a pharmaceutically acceptable carrier, vehicle or diluent.
39. A pharmaceutical combination composition comprising: a therapeutically effective amount of a composition comprising
- 25 a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug;
- 30 a second compound, said second compound being a lipase inhibitor, an HMG-CoA reductase inhibitor, an HMG-CoA synthase inhibitor, an HMG-CoA reductase gene expression inhibitor, an HMG-CoA synthase gene expression inhibitor, an MTP/Apo B secretion inhibitor, a CETP inhibitor, a bile acid absorption inhibitor, a cholesterol absorption inhibitor, a cholesterol synthesis inhibitor, a squalene synthetase inhibitor, a squalene epoxidase inhibitor, a squalene cyclase inhibitor, a combined squalene epoxidase/squalene cyclase inhibitor, a fibrate, niacin,

an ion-exchange resin, an antioxidant, an ACAT inhibitor or a bile acid sequestrant; and

a pharmaceutically acceptable carrier, vehicle or diluent.

40. A pharmaceutical combination composition as recited in claim 39 wherein the
5 second compound is an HMG-CoA reductase inhibitor or a CETP inhibitor.
41. A pharmaceutical combination composition as recited in claim 39 wherein the
second compound is rosuvastatin, itavastatin, lovastatin, simvastatin, pravastatin,
fluvastatin, atorvastatin or rivastatin or a pharmaceutically acceptable salt thereof.
42. A method for treating atherosclerosis in a mammal comprising administering to a
10 mammal in need of treatment thereof;
- 15 a first compound, said first compound being a compound of claim 1, a
prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said
prodrug; and
- 20 a second compound, said second compound being a lipase inhibitor, an
HMG-CoA reductase inhibitor, an HMG-CoA synthase inhibitor, an HMG-CoA
reductase gene expression inhibitor, an HMG-CoA synthase gene expression
inhibitor, an MTP/Apo B secretion inhibitor, a CETP inhibitor, a bile acid absorption
inhibitor, a cholesterol absorption inhibitor, a cholesterol synthesis inhibitor, a
squalene synthetase inhibitor, a squalene epoxidase inhibitor, a squalene cyclase
inhibitor, a combined squalene epoxidase/squalene cyclase inhibitor, a fibrate, niacin,
an ion-exchange resin, an antioxidant, an ACAT inhibitor or a bile acid sequestrant
wherein the amounts of first and second compounds result in a therapeutic
effect.
- 25 43. A method for treating atherosclerosis as recited in claim 42 wherein the second
compound is an HMG-CoA reductase inhibitor or a CETP inhibitor.
44. A method for treating atherosclerosis as recited in claim 42 wherein the second
compound is rosuvastatin, itavastatin, lovastatin, simvastatin, pravastatin, fluvastatin,
atorvastatin or rivastatin or a pharmaceutically acceptable salt thereof.
45. A kit comprising:
30 a. a first compound, said first compound being a compound of claim 1, a
prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said
prodrug and a pharmaceutically acceptable carrier, vehicle or diluent in a first unit
dosage form;

- b. a second compound, said second compound being a lipase inhibitor, an HMG-CoA reductase inhibitor, an HMG-CoA synthase inhibitor, an HMG-CoA reductase gene expression inhibitor, an HMG-CoA synthase gene expression inhibitor, an MTP/Apo B secretion inhibitor, a CETP inhibitor, a bile acid absorption inhibitor, a cholesterol absorption inhibitor, a cholesterol synthesis inhibitor, a squalene synthetase inhibitor, a squalene epoxidase inhibitor, a squalene cyclase inhibitor, a combined squalene epoxidase/squalene cyclase inhibitor, a fibrate, niacin, an ion-exchange resin, an antioxidant, an ACAT inhibitor or a bile acid sequestrant and a pharmaceutically acceptable carrier, vehicle or diluent in a second unit dosage form; and
- 5 c. means for containing said first and second dosage forms
10 wherein the amounts of first and second compounds result in a therapeutic effect.
46. A kit as recited in claim 45 wherein said second compound is an HMG-CoA
15 reductase inhibitor or CETP inhibitor.
47. A kit as recited in claim 45 wherein said second compound is rosuvastatin,
itavastatin, lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or rivastatin or
a pharmaceutically acceptable salt thereof.